

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A composition for generating a complex-forming metal ion labeled agent, the composition comprising:

- (a) a metal support surface which is made of gold, silver or copper, or which is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic polystyrene, polyacrylamide, Sephadex, and agarose; and
- (b) a conjugate releasably bound to the support surface, the conjugate comprising a ligand and a targeting molecule;

wherein the conjugate coordinates with a complex-forming metal ion so that the labeled conjugate is released from the support surface.

2. (Previously presented) The composition of claim 1, wherein the metal support surface releasably coordinates to sulfur or phosphorous and the ligand comprises a sulfur or phosphorous atom for binding to the metal support surface.

3. (Previously presented) The composition of claim 2, wherein the ligand comprises a sulfur atom attached to a sulfur protecting group, wherein the metal support surface binds to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the ligand.

4. (Previously presented) The composition of claim 2, wherein the conjugate comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

5. (Original) The composition of claim 4, wherein the conjugate comprises a peptide sequence selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM (SEQ ID NO:1), TKPPR (SEQ ID NO:2) and RGDS (SEQ ID NO:3).

6. (Original) The composition of claim 4, wherein the conjugate comprises a small organic molecule that targets a receptor or a transporter.

7. (Currently amended) The composition of claim 2, wherein the ligand comprises:

(a) a surface binding group selected from the group consisting of a cysteine amino acid residue, ~~a cysteine amino acid residue derivative~~, a thiol or thioester group attached to an organic molecule, an amino acid residue, ~~an amino acid residue derivative including phosphorous~~ and a phosphorous containing organic molecule, wherein the amino acid residue, ~~amino acid residue derivative~~ or organic molecule binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion.

8. (Previously presented) The composition of claim 7, wherein the ligand comprises a peptide, a peptide mimetic, a polypeptide, a polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

9. (Currently amended) The composition of claim 8, wherein the ligand comprises a peptide selected from the group consisting of a tetradentate N_xS_{4-x} ligand, ~~a tetradentate N_xS_{4-x} ligand derivative where $x = 0$ to 3, and~~ a polyamino polysulfide ~~and a polyamino polysulfide~~

derivative.

10. (Currently amended) The composition of claim 8, wherein the ligand comprises 3 accessory groups, each selected from the group consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more of (a) to (c), wherein the residues, ~~derivatives~~ and/or molecules have metal coordinating activity.

11. (Previously presented) The composition of claim 1, wherein the targeting molecule comprises a molecule having agonist or antagonist activity selected from the group consisting of a polypeptide, a peptide, a nucleic acid molecule, an oligonucleotide, a saccharide, an oligosaccharide, a steroid, a cyclic peptide, a peptide or polypeptide mimetic, an enzyme substrate, an inhibitor and an organic molecule having a molecular weight less than about 600 Daltons.

12. (Previously presented) The composition of claim 1, wherein the targeting molecule comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

13. (Previously presented) The composition of claim 1, wherein the targeting molecule comprises a molecule selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM (SEQ ID NO:1), TKPPR (SEQ ID NO:2), RGDS (SEQ ID NO:3) and an organic molecule having a molecular weight less than about 600 Daltons that targets a receptor or a transporter.

14. (Previously presented) The composition of claim 6 or claim 13, wherein the receptor or transporter is selected from the group consisting of a dopamine receptor or

transporter, a serotonin receptor or transporter, a sigma receptor, GABA receptor, a nicotinic receptor, a cholinergic receptor, a norepinephrine receptor or transporter, a glucose transporter and an opioid receptor.

15. (Cancelled)

16. (Previously presented) The composition of claim 3, wherein the metal support surface comprises gold.

17. (Currently amended) The composition of claim 1-5, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

18. (Previously presented) The composition of claim 17, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Cu and Re.

19. (Previously presented) A method for generating a complex-forming metal ion labeled diagnostic agent or radiotherapeutic agent, comprising: (a) providing a composition according to claim 1; and (b) contacting the composition with the complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the agent so that the complex-forming metal labeled agent is released from the support surface.

20. (Previously presented) The method of claim 19, further comprising collecting the complex-forming metal labeled agent so released.

21. (Previously presented) A metal ion labeled agent prepared using a composition of claim 1.

22. (Previously presented) A technetium or rhenium labeled agent prepared using a composition of claim 1, wherein the agent is labeled with ^{99m}Tc and has a specific activity of

greater than 10,000 Ci/mmol or the agent is labeled with ^{188}Re and has a specific activity of greater than 3,000 Ci/mmol.

23. (Original) The composition of claim 22, wherein the agent is a peptide comprising dimethylglycylserinylcysteinylglycine.

24. (Previously presented) A pharmaceutical composition for radiotherapy or imaging, comprising a carrier and a complex-forming metal ion labeled agent, wherein the agent is prepared using a composition of claim 1.

25. (Original) The pharmaceutical composition of claim 24 further comprising at least one agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilizing agent.

26. (Previously presented) A method of detecting the presence or assessing the severity of an oncological, neurological, inflammatory, infectious and degenerative disease, disorder or abnormal physical state in a mammal comprising:

(a) administering an effective amount of the agent or composition of claim 22 or claim 24; and

(b) detecting the presence or assessing the severity of the disease, disorder or abnormal physical state.

27. (Previously presented) A method of radiotherapy of a disease, disorder or abnormal physical state in a mammal comprising administering an effective amount of the agent or composition of claim 22 or claim 24.

28. (Previously presented) The method of claim 26, wherein the complex-forming metal labeled imaging agent is administered by an intravenous route.

29. (Previously presented) The method of claim 26, wherein the amount of complex-

forming metal labeled agent administered to the mammal is about 0.01 mcg/kg/minute to 1,000 mcg/kg/minute.

30. (Original) The method of claim 29, wherein the amount of the complex-forming metal labeled agent administered to the mammal is about 0.01 to 50 mcg/kg/minute.

31. (Previously presented) The method of claim 26, wherein the mammal is a human.

32. (Cancelled)

33. (Previously presented) The method of claim 26, wherein the presence or the severity of a disease, disorder or abnormal physical state is detected or assessed with a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast X-ray computed tomography, and digital subtraction angiography.

34. (Previously presented) The method of claim 33, wherein the agent comprises a ^{99m}Tc metal and binds to a receptor and the technique is single photon emission computed tomography.

35. (Currently amended) A kit for preparing a complex-forming metal ion labeled agent, the kit comprising a metal support surface, conjugate and a predetermined quantity of complex-forming metal ion, the conjugate being releasably bound to the support surface and which coordinates with the complex-forming metal ion so that the conjugate is released from the metal support surface,

wherein said metal support surface is made of gold, silver or copper, or is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic

polystyrene, polyacrylamide, Sephadex, and agarose.

36. (Previously presented) The kit of claim 35, wherein the conjugate comprises a sulfur atom attached to a sulfur protecting group, wherein the metal support surface binds to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the conjugate.

37. (Previously presented) The kit of claim 35, wherein the metal support surface releasably coordinates to sulfur or phosphorous and the conjugate comprises a sulfur or phosphorous atom for binding to the metal support surface.

38. (Currently amended) The kit of claim 27, wherein the conjugate comprises a ligand and a targeting molecule, wherein the ligand comprises:

(a) a surface binding group selected from the group consisting of a cysteine amino acid residue, ~~a cysteine amino acid residue derivative~~, a thiol or thioester group attached to an organic molecule having a molecular weight less than about 600 Daltons, ~~an amino acid residue derivative including phosphorous~~ and a phosphorous containing organic molecule, wherein the amino acid residue, ~~amino acid residue derivative~~ or organic molecule releasably binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion.

39. (Currently amended) The kit of claim 35, wherein ~~the metal support surface comprises a metal selected from the group consisting of gold, silver, copper and a metal that binds sulfur or phosphorous for forming a metal complex; and~~ the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni,

Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

40. (Previously presented) The kit of claim 39, further comprising at least one agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilizing agent.

41. (Currently amended) A method for generating a complex-forming metal ion labeled agent comprising:

(a) providing a metal support surface which is made of gold, silver or copper, or which is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic polystyrene, polyacrylamide, Sephadex, and agarose;

(b) providing a conjugate comprising a ligand and targeting molecule, wherein the ligand comprises a peptide, a peptide mimetic, a polypeptide or a polypeptide mimetic of about 3 to 50 amino acid residues ~~or derivatives thereof~~ and includes a sulfur atom for binding to the metal support surface, the sulfur atom being protected by a sulfur protecting group;

(c) contacting the protected sulfur atom with the metal support surface so that the sulfur atom forms a thiol bond with the metal surface thereby releasing the sulfur protecting group; and

(d) contacting the ligand with the complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the ligand so that the complex-forming metal labeled agent is released from the support surface.

42. (Currently amended) The method of claim 41, wherein ~~the metal support surface~~

~~comprises a metal selected from the group consisting of gold, silver, copper and a metal that releasably binds sulfur or forms a metal complex; and~~ the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

43 - 44. (Cancelled)

45. (Previously presented) The composition of claim 1, wherein the ligand comprises an organic molecule having a molecular weight of less than about 600 Daltons, which comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorous atom where the sulfur or phosphorous atom binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion.

46. (Previously presented) The kit of claim 27, wherein the conjugate comprises a ligand and a targeting molecule, wherein the ligand comprises an organic molecule having a molecular weight of less than about 600 Daltons, which comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorous atom where the sulfur or phosphorous atom binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion.

47. (Previously presented) A method of detecting the presence or assessing the severity of a disease in a mammal selected from the group consisting of an oncological disease, a neurological disease, an inflammatory disease and an infection, comprising:

(a) administering an effective amount of an agent or composition of claim 22 or claim 24; and

(b) detecting the presence or assessing the severity of the disease

48. (Previously presented) A method of radiotherapy of a disease in a mammal selected from the group consisting of an oncological disease, a neurological disease, an inflammatory disease and an infection, comprising administering an effective amount of the agent or composition of claim 22 or claim 24.

49. (Previously presented) The method of claim 26, wherein the presence or severity of the disease is detected or assessed with a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast X-ray computed tomography, and digital subtraction angiography